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Discussant
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Acute Renal Failure

STANLEY A. MENDOZA:* Children with acute renal failure are gravely ill but in most cases can recover completely. Good medical management can make the difference between survival with complete recovery and death of the child. I plan to emphasize the treatment of children with acute renal failure. However, I will begin with definition of acute renal failure, followed by a discussion of its causes, incidence and prognosis.

Acute renal failure is the sudden, progressive loss of renal function. Oliguria is common in children with acute renal failure, but it is not always present. There are a number of children who present with virtually complete loss of renal function but with a sizable urine output.

There are prerenal, renal and postrenal causes of acute renal failure. Gastroenteritis is the most common of the prerenal causes. Children with this condition respond well to treatment in virtually all cases. Other prerenal causes of acute renal failure are burns, hemorrhages, hypotension and renal artery obstruction.

There are a number of parenchymal renal diseases that can cause acute renal failure. The three most common are acute poststreptococcal glomerulonephritis, hemolytic uremic syndrome and acute tubular necrosis. At one time the most common renal parenchymal disease that caused acute renal failure in children was poststreptococcal acute glomerulonephritis. This is no longer true, at least in the area of our institution. There is no obvious explanation for this trend. There are many children with streptococcal infections. In addition, in a significant number of children acute poststreptococcal glomerulonephritis develops, although in perhaps fewer than in the past. However, the disease is usually milder than in the past, and it is unusual to see a child with severe acute renal failure from poststreptococcal glomerulonephritis.

Hemolytic uremic syndrome (HUS) is a condition that usually begins with bloody diarrhea. Three days to a week later, extreme pallor and acute renal failure suddenly develop, usually associated with anuria and thrombocytopenia. There is a significant geographic variation in the severity of this syndrome. In California, 80 to 90 percent of the children with HUS recover completely.[1,2] These children are often hypertensive and may be anuric for periods of up to three weeks, but they usually recover completely. HUS was first described in 1955.[3] Until dialysis become generally available, a child with severe acute renal failure due to HUS would almost certainly have died. Consequently, the longest follow-up in these children is 10 to 12 years. During that time, the children who have apparently recovered completely from their acute illness have remained well. It seems likely that these children do not have residual damage to the kidneys, but there is no way to be sure that chronic renal disease will not evolve later.

Patients with poor renal perfusion due to dehydration, burns, hemorrhage or hypotension have a condition which can be immediately reversed if renal perfusion is improved. If the hypoperfusion of the kidney continues long enough, there can be parenchymal damage and acute tubular necrosis (ATN). This is probably the most com-

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ABBREVIATIONS USED IN TEXT

ASO = antistreptolysin-O
ATN = acute tubular necrosis
GFR = glomerular filtration rate
HUS = hemolytic uremic syndrome

TABLE 1.—*Potentially Lethal Complications of Acute Renal Failure*

- Circulatory overload
- Hypertensive encephalopathy
- Hyperkalemia
- Uremia
- Infection

mon of the causes of acute renal failure in children, particularly in intensive care nurseries, where infants are frequently hypoxic and hypotensive for varying periods of time. If that period is sufficiently long, ATN develops. This is also a potentially reversible disease.

Of the postrenal causes of acute renal failure, the most common is obstructive uropathy. If the diagnosis is made early enough, there is a potential for complete or nearly complete recovery of renal function unless the obstruction is associated with renal dysplasia.

The most common causes of acute renal failure, therefore, are dehydration, acute poststreptococcal glomerulonephritis, hemolytic uremic syndrome, acute tubular necrosis and obstructive uropathy. Each has a good prognosis if the child is treated properly during the acute illness. There is no specific treatment for the parenchymal causes of acute renal failure, acute tubular necrosis, hemolytic uremic syndrome or acute poststreptococcal glomerulonephritis. Basically, what must be done is to support the patient until he recovers spontaneously. The treatment of these children is designed to prevent or reverse the potentially lethal complications of acute renal failure. These are listed in Table 1. I shall discuss the cause, prevention and treatment of each of these complications.

Circulatory overload in children with acute renal failure results from the retention of salt and water. The diseased kidney is unable to maintain homeostasis. If salt and water overload are prevented in a child with acute renal failure, the signs of circulatory overload will not develop. Thus, prevention of circulatory overload is really quite simple. The patient should be given no salt and very little water. The implication of this statement is that acute renal failure is usually not associated with intrinsic cardiac disease.

Existing circulatory overload is difficult to treat. These children may present with a gallop rhythm, pulmonary edema, cardiomegaly, hepatomegaly and peripheral edema. Classical methods of treating congestive heart failure such as phlebotomy, rotating tourniquets, use of oxygen, bed rest, elevating the bed and morphine administration should be used.

It must be emphasized that digitalis is contraindicated. In these patients, the load on the heart progressively increases due to salt and water retention. The heart responds to this increased load by increasing contractility in accordance with Starling's law. Cardiac contractility increases until the load gets so great that a further increase in contractility is impossible and circulatory overload results. Digitalis acts by increasing cardiac contractility. Since the heart is incapable of further increasing contractility, digitalis is ineffective. Thus, one reason not to use digitalis is that it does not work. Digitalis has, in fact, been given to a large number of patients with acute renal failure and circulatory overload. It is usually ineffective. The major reason for not using digitalis, however, is that it is extremely dangerous. Digitalis is mainly excreted by the kidney. Therefore, it is easy to produce digitalis intoxication in a patient with impaired renal function. Furthermore, management of digitalis intoxication in a patient with acute renal failure is extremely difficult. The usual treatment for digitalis intoxication is intravenous administration of potassium, which is extremely dangerous in a child with renal dysfunction. In addition, digitalis is not dialyzable, so that if a patient becomes digitalis intoxicated the drug can not be easily removed. In fact, dialysis tends to make the digitalis intoxication worse because potassium is removed by dialysis, thereby potentiating the effect of digitalis. I have seen two children in whom severe arrhythmias developed after the use of digitalis in acute renal failure. I feel very strongly that it is contraindicated in almost all cases. The exceptions to this rule are the patients who have acute renal failure and intrinsic cardiac disease. In these cases, digitalis may be indicated because it can improve cardiac contractility. In such cases, digitalis should be administered extremely carefully with frequent electrocardiograms and measurement of blood levels of digitalis.

Diuretics are frequently ineffective in patients with acute renal failure due to parenchymal renal disease. Diuretics act by decreasing the sodium chloride reabsorptive capacity of some part of the nephron. Thus, more sodium chloride and water are excreted. Patients with severe acute renal failure due to parenchymal renal disease may have a very low glomerular filtration rate (GFR). Obviously, if the GFR is sufficiently low, decreasing tubular reabsorption will not increase urinary sodium and water excretion. Consequently, many patients with acute renal failure do not respond to diuretics. However, some patients with acute renal failure and circulatory overload do respond well to a diuretic such as ethacrynic acid or furosemide. Even a small diuresis can be sufficient to make a dramatic difference in the clinical course of a patient with circulatory overload. The heart rate slows, the gallop rhythm disappears and oxygenation improves. Of course, this is the reason that phlebotomy is a part of standard therapy. Phlebotomy is another way to remove volume acutely from the plasma. Ethacrynic acid or furosemide is indicated in children with acute renal failure and circulatory overload. In a normal person each may cause the excretion of as much as 20 percent of the filtered sodium. Side effects are minimal. Both of these drugs can cause deafness. In the case of furosemide, I am unaware of irreversible deafness. There are reports of irreversible deafness due to use of ethacrynic acid.[4] The major reported side effect of both ethacrynic acid and furosemide is imbalance of fluid and electrolytes caused by excessive loss of water and salt. In a child with severe circulatory overload and acute renal failure, it would be delightful to have to worry about replacing excessive salt and water loss. Since these diuretics occasionally work dramatically and are relatively innocuous, they should be tried.

Peritoneal dialysis or hemodialysis is quite effective in treating patients with acute renal failure and circulatory overload. In practical terms, it takes one to two hours to start an emergency peritoneal dialysis or to arrange surgical vascular access before hemodialysis. In a child with acute renal failure, and circulatory overload, I start with phlebotomy, rotating tourniquets, oxygen, diuretics and morphine, but at the same time, I begin organizing emergency dialysis. In one to two hours when the dialysis can begin, the patient will either have improved significantly with conservative management or not. If he has, conservative management can be continued without dialysis. If he has not improved significantly, then dialysis can begin immediately.

A second potentially lethal complication of acute renal failure is hypertensive encephalopathy. There are several causes of hypertension in patients with acute renal failure. The most significant cause is retention of salt and water. If retention of salt and water are prevented, hypertension will usually not be severe. Renal vascular disease can also occur with impairment of renal perfusion. This can result in the release of renin by the kidney. Renin then causes a protein in the blood to be converted to angiotensin I and II. Angiotensin II is an extremely powerful pressor agent. The renal parenchymal causes of renal acute failure can increase plasma renin activity.

A child we saw recently was of particular interest because he presented in an unusual manner, with an acute onset of blindness. His eyegrounds were normal initially but his blood pressure was 220/160 mm of mercury. An EMI® scan done early in the course of the illness showed a decrease in perfusion to the occiput, where the visual cortex is located. When the abnormal blood pressure was adequately treated, his vision returned. We thought he had hypertensive encephalopathy localized to the occiput. On the third hospital day his blood pressure rose again, and during this rise the patient again became blind. Fortunately when hypertension was treated, vision returned, and he is now perfectly normal. This boy had acute poststreptococcal glomerulonephritis with abnormal findings on urinalysis, an elevated antistreptolysin-O (ASO) titer and low serum complement. Another child with acute poststreptococcal glomerulonephritis presented with a generalized seizure. His blood pressure was 240/180 mm of mercury, and he had florid hypertensive retinopathy. He did well after receiving antihypertensive therapy.

Severe hypertension is life-threatening. In patients with acute renal failure, severe hypertension can usually be prevented by careful monitoring of the intake of salt and water. Antihypertensive drugs are indicated. When the blood pressure is notably elevated a parenteral agent which acts rapidly is indicated. In general the initial drug of choice is hydralazine. When given intravenously, this drug acts rapidly and can be repeated every 15 minutes until the blood pressure falls.

In a true hypertensive emergency even hydralazine may act too slowly. In such a case the

best drugs are diazoxide and nitroprusside. Diazoxide is given by rapid intravenous injection in a dose of 2 to 5 mg per kg of body weight. The blood pressure usually falls rapidly after diazoxide administration. An effect is generally seen within five minutes, often in one to two minutes. One dose is usually effective for 6 to 12 hours, and the drug can be repeated. Nitroprusside is given by intravenous drip. The infustion rate is slowly increased until the blood pressure falls. One problem with nitroprusside is that it is unstable in light. For this reason, the IV bottle and tubing must be wrapped in a light resistant material such as aluminum foil. When diazoxide or nitroprusside is used, it is important to begin oral antihypertensive therapy at the same time to provide long-term control of blood pressure. Dialysis can be used to treat hypertension in acute renal failure since salt and water overload is a major cause of the hypertension. In a severe hypertensive emergency, dialysis is too slow. As mentioned earlier, it usually takes one or two hours to start the dialysis. Another one or two hours pass before the dialysis significantly affects the blood pressure. Therefore, the initial treatment is with antihypertensive drugs. Dialysis can be useful in keeping the blood pressure down.

A third cause of death in patients with acute renal failure is electrolyte imbalance, especially hyperkalemia. Although these patients can have acidosis, hypocalcemia, hyperphosphatemia, hyponatremia or hypernatremia, the major life-threatening change in serum electrolytes is an elevation in the serum concentration of potassium. Hyperkalemia in patients with acute renal failure is caused by dietary intake of potassium and tissue breakdown. These patients are seriously ill and are catabolic. As tissue is broken down, large amounts of potassium are released because intracellular concentrations of potassium are high. Another cause of hyperkalemia is the administration of blood, particularly old blood. When blood is stored, the potassium from the red cells leaks into the plasma. The plasma potassium concentration of such blood can be 15 to 20 mEq per liter. In addition some patients with acute renal failure, especially those with HUS, have significant hemolysis releasing potassium into the plasma.

Hyperkalemia can be prevented in several ways. First the patient with acute renal failure needs absolutely no potassium intake. The most significant route by which the body loses electrolytes is the urine. If a patient is anuric, electrolyte losses are minimal. In anuric patients the major problems with electrolytes occur when too much is given. Thus too much sodium causes circulatory overload and hypertension. Too much potassium causes dangerous hyperkalemia. It is difficult to give too little sodium or potassium to an anuric patient. Second, caloric intake should be encouraged. If 20 to 25 percent of the daily calorie requirements are taken, either as carbohydrate or fat, protein catabolism is decreased, thus decreasing the release of potassium from cells. This also slows the rate of increase in the blood urea nitrogen. Third, only fresh blood should be given. The serum potassium concentration in fresh blood is low. Further, packed cells should be infused since this decreases the volume of potassium-containing plasma administered as well as decreasing the total volume infused, thereby decreasing the risk of producing circulatory overload or severe hypertension. If a transfusion is necessary, only buffy coat poor or frozen red cells should be used. Although most such patients recover, some do not. Therefore, any patient with acute renal failure should be regarded as a potential candidate for a renal transplant. Buffy coat poor or frozen red cells significantly decrease the risk of sensitizing the patient to foreign antigens.

TABLE 2.—*Methods of Treating Hyperkalemia*

Agent	*Onset of Effect*	*Duration of Effect*
Calcium gluconate ...	< 5 minutes	30-60 minutes
Sodium bicarbonate ..	< 5 minutes	1-2 hours
Insulin and glucose ..	20-30 minutes	2-4 hours
Kayexalate	1-2 hours	4-6 hours
Dialysis	Variable	Variable

Table 2 lists methods of treating hyperkalemia in order of their onset and duration of action. Calcium and sodium bicarbonate work extremely rapidly. The electrocardiographic changes of hyperkalemia improve dramatically in one to two minutes. Calcium acts by antagonizing the effects of potassium on cardiac muscle. Bicarbonate acts by releasing hydrogen ions from the cells in exchange for potassium ions. Neither calcium nor bicarbonate removes potassium from the body in a patient with renal failure. Therefore, their effects tend to be brief, usually lasting about one hour. Since calcium and bicarbonate are short acting, their use is only indicated in a patient with an arrhythmia due to severe hyperkalemia. If the patient has a high serum potassium concentration and peaked T waves but no arrhythmia, insulin and glucose may be given. Insulin causes

the uptake of glucose by muscle cells. Potassium is taken up with the glucose. Therefore, insulin and glucose remove potassium from the plasma, thereby improving the patient's general status, but do not remove potassium from the body. It is generally stated that it takes 20 to 30 minutes for insulin and glucose to work, but I have seen improvement on electrocardiograms in less than five minutes after insulin and glucose administration.

The two forms of therapy for hyperkalemia which remove potassium from the body are the ion-exchange resin, polystyrene sulfonate (Kayexalate®) and dialysis. Kayexalate is given either orally or rectally in the sodium form. The affinity of the resin is higher for potassium than for sodium. Sodium is exchanged for potassium and the potassium-containing resin is excreted in the stools. One potential complication of Kayexalate therapy is that for each potassium ion removed from the body, one sodium ion is added. This can cause salt and water overload while the hyperkalemia is improving. Dialysis is an extremely effective way of removing potassium from these patients.

The fourth cause of death in acute renal failure is uremia. The uremic syndrome includes many problems but the life-threatening complications are neurologic, including lethargy, coma and seizures. There is a great deal of debate in the literature as to the nature of the uremic toxin or toxins. There are a number of complications of uremia including peripheral neuropathy, pericarditis, neurologic symptoms, myopathy and others. It is not clear whether a single toxin causes all of these complications, or if there is a different toxin for each. It is generally assumed that the toxin or toxins are tissue breakdown products, possibly nitrogen-containing tissue breakdown products but even this is unproven. The onset of uremic symptoms can apparently be delayed by minimizing tissue breakdown by giving adequate calories. Dialysis will treat or prevent the neurological complications of acute renal failure. Presumably some toxin or toxins are removed by dialysis.

The fifth cause of death in acute renal failure is infection. In some series of adults, infection was the most common cause of death in patients with acute renal failure. Uremic patients have decreased resistance to infection because of defects in both humoral and cellular immunity. A second cause of infection is that these patients are often lethargic or comatose. They tend to lie flat in bed and decubitus ulcers, hypostatic pneumonia or other opportunistic infections which occur in severely ill patients can develop. This risk can be minimized by excellent nursing care with appropriate turning of patients and respiratory therapy. A third cause of infection in these patients is the use of indwelling urinary catheters. The only information that an indwelling catheter provides is an hour-by-hour measure of urine output. This information is therapeutically worthless. It is clinically relevant to know if urine output is high or low. This information is available without using an indwelling catheter since if urine output is high the patient will either void or develop a full bladder. An indwelling urinary catheter is particularly dangerous in patients with a low urinary output. A patient with an indwelling urinary catheter and a high urine volume may wash out bacteria which enter the bladder. If urine output is low, the bacteria which enter the bladder multiply without significant washout. Therefore, the use of an indwelling urinary catheter should be avoided. There is an occasional reason for an in-and-out bladder catheterization to determine urine output or to obtain urine for culture. This is an essentially benign procedure if done carefully. Indwelling catheters are not benign.

TABLE 3.—*Therapy for Oliguric Patients*

- Water—calculated insensible loss plus urine output.
- Sodium—replacement of urinary loss.
- Potassium—none
- Calories—at least 20 to 25% of daily requirement, as carbohydrate and/or fat.

A high index of suspicion is necessary to recognize infection. If infection is suspected, antibiotics should be given after appropriate cultures are obtained. Since many antibiotics are nephrotoxic or excreted by the kidney, or both, modification of dosage schedules may be necessary.

Table 3 is a proposed treatment regimen for oliguric patients. Recommended fluid intake is insensible loss plus the urine output. If the patient is initially somewhat volume overloaded, he should be given less fluid than this so that total levels of body water will return to normal. Virtually all fluid volume problems in patients with acute renal failure are due to volume overload. Therefore, if there is any question about the volume of fluid to be given, the smaller volume should be used.

TABLE 4.—*Indications for Dialysis in Acute Renal Failure*

- Severe circulatory overload
- Severe hypertension
- Hyperkalemia
- Uremic symptoms

Sodium losses can be estimated by measuring urine volume and urinary sodium concentrations unless the patient has either cystic fibrosis with a high salt concentration in the sweat or gastrointestinal losses. Most problems result from giving too much sodium. No sodium should be given to anuric patients. Urinary potassium excretion can be monitored and potassium loss replaced. Here again, patients with acute renal failure are more likely to have problems with potassium overload than with potassium depletion. At least 20 to 25 percent of the estimated caloric requirements should be given as carbohydrates or fats.

Table 4 lists the indications for dialysis in acute renal failure. The resemblance between this list and the listing in Table 1 of the causes of death in patients with acute renal failure is intentional. The indication for dialysis in these patients is any complication of uremia which is unresponsive to conservative management.

If one treats a patient with acute renal failure appropriately and does dialysis when indicated, the chance of the patient surviving the acute illness is very high. If the acute illness is ATN, HUS or acute poststreptococcal glomerulonephritis, the probability is extremely high, perhaps 80 to 90 percent, that this recovery will be complete.

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Cholecystitis in Patients with Diabetes

The occurrence of acute cholecystitis in patients with diabetes deserves special mention. In the presence of diabetes, perforation of the gallbladder is more frequent, and it often occurs within 72 hours of the onset of the disease. Most important, the mortality rate of acute cholecystitis in those with diabetes is high: it ranges from 8 percent to 22 percent. For these reasons, there really is no place for nonoperative treatment. In patients with diabetes, an operation should be undertaken with dispatch as soon as the diagnosis is made.

—MARSHALL J. ORLOFF, MD, *San Diego*
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